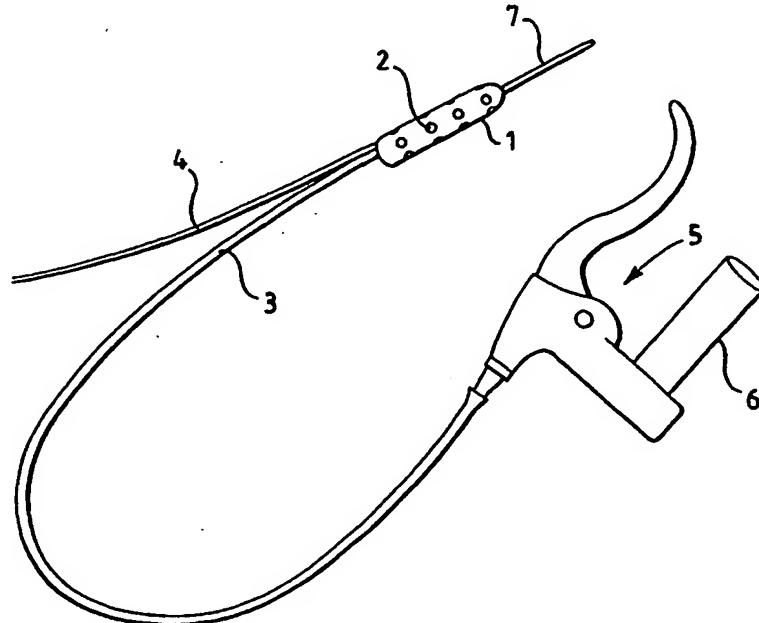


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(54) Title: DEVICE FOR REMOVING SURFACE TISSUE, IN PARTICULAR FOR TAKING BIOPSIES



(57) Abstract

A device for taking biopsies comprises a cutting head (1) having a surface in which are defined a plurality of recesses (2). Suction is provided to the recesses to draw tissue therein, and the drawn in tissue is severed to form biopsies, each of which is held in a respective recess (2). The severing is performed by relative movement between an inner core (12) and an outer sheath (13) of the cutting head (1).

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**DEVICE FOR REMOVING SURFACE TISSUE,
IN PARTICULAR FOR TAKING BIOPSIES**

This invention relates to a device for taking biopsies and is particularly concerned
5 with a device for taking a plurality of biopsies, more particularly for taking a plurality of biopsies from patients with Barrett's oesophagus. Barrett's oesophagus is a pre-malignant condition in which specialized intestinal metaplasia occurs in gastric mucosa which has developed in the oesophagus, usually as a result of chronic gastro-oesophageal reflux disease. There is a need for multi biopsy for surveillance to try and pick up patients in whom high
10 grade dysplasia and earlier cancer occur, so that they can receive early treatment. The incidence of cancer in patients with Barrett's oesophagus is about 10%. Segments of Barrett's oesophagus may extend from 3 to 10 centimetres or more above the gastro-oesophageal junction. Segments of Barrett's oesophagus shorter than 3 cms used to be regarded as a normal finding at endoscopy but probably also have a risk of progression to
15 cancer. It has been recommended that biopsies are taken from four quadrants of Barrett's oesophagus at either 1 or 2 centimetre intervals on alternate years for histological assessment to look for changes such as dysplasia which may predict or indicate the development of cancer.

20 There have been recent recommendations by the World Congress of Gastroenterology on screening for Barrett's. It is likely that more biopsies are going to be taken from patients with Barrett's and there is going to be considerably more interest in this condition in future years. The current problem with endoscopic biopsies is that it takes 2 or 3 minutes to take each biopsy and, so taking multiple biopsies from the oesophagus is time consuming. It is

also difficult to be precise about where in the oesophagus the biopsies have come from.

Devices are known for taking a plurality of biopsies, but none of these enables the locations from which the biopsies have come to be reliably related to the biopsies themselves, 5 and none enables a plurality of biopsies to be taken simultaneously. Such known devices are described, for example, in US Patents 4651753 and 5601585.

According to the present invention there is provided a device for taking biopsies, which comprises a cutting head having a surface in which are defined a plurality of recesses, 10 means for communicating suction to the recesses to draw tissue therein, and means for severing the drawn in tissue to form biopsies each of which is held in a respective recess.

The device according to the invention can be used to take multiple biopsies from the oesophagus in an oriented fashion, and retain the biopsies in their orientation so that the 15 pathologist can examine these in a numbered sequence which relates to the pathology, e.g. with the first biopsy coming from the lowest margin of the Barrett's segment oriented at 12 o'clock and with the other biopsies being related precisely to the orientation of the biopsy position.

20 Preferably, the cutting head comprises a core which includes the recesses for holding the biopsies and an outer sheath which includes a plurality of openings for cooperation with the recesses, the core and the sheath being axially slidable with respect to each other to perform the severing operation.

The invention is further described below with reference to the accompanying drawings, in which:

5 Figure 1 is a perspective view of one embodiment of the device;

Figure 2 shows schematically one form of cutting head for use in the device and the components making up the head;

10 Figure 3a and 3b show in greater detail the cutting head of Figure 2, in longitudinal section, before and after taking biopsies, respectively;

Figure 4 shows another form of cutting head for use in the device;

15 Figure 5 shows a further form of cutting head for use in the device, and the components making up the device; and

Figure 6 shows, in a cutaway view, a component of which a plurality can be assembled to make a complete cutting head.

20 As shown in Figure 1, the device comprises a cutting head 1, having a plurality of recesses 2 in its surface. The illustrated device is one which has four longitudinally extending rows of recesses, with four recesses in each row, i.e. sixteen recesses in all, with the recesses in each row being aligned axially with the corresponding recesses in the other rows. However, it is to be understood that other patterns can be used, involving more or

fewer recesses, and either aligned or offset with respect to one another.

In the example shown in Figure 1, one end of the cutting head, which forms its proximal end, is attached to the distal end of a wire/sheath cable 3, commonly known as a 5 Bowden cable. The proximal end of the cable 3 is connected to a handle 5 which is operated in basically the same way as the handle of a bicycle brake (which also employs a Bowden cable). An additional hollow tube 6 may be mounted on the handle 5 to provide a storage receptacle for the cutting head when it is not in use. The proximal end of the cutting head is also connected to a tube 4 for carrying suction to the head. However, instead of a separate 10 tube 4, the suction could be conveyed through the Bowden cable, using the region between the wire and the sheath. In that case an air tight seal would need to be provided around the wire where it enters the handle 5 to prevent air being inadvertently sucked into the sheath of the Bowden cable from a region other than that intended. The distal end of the cutting head 1 may be fitted with a resiliently flexible guide member 7 to assist in guiding the head 15 when it is inserted in the patient's body.

Turning now to Figure 2, this shows schematically one embodiment of cutting head. The complete head 11 is shown in Fig. 2a, the head 11 with the outer tube 13 removed to reveal the core 12 is shown in Fig. 2b (Fig. 2c is a cross-section through the core). The 20 outer tube 13 of the head is shown in Fig. 2d, and Fig. 2e shows an optional split sleeve 14 (Fig. 2f is a cross-section through the sleeve of Fig. 2e).

The main body of the core 12 is generally tubular in form, and may be of metal, preferably stainless steel or brass. Typically, the core has an outside diameter of 14mm.

The core has a plurality of parallel longitudinally extending rows of recesses 15 in the surface thereof, the particular example here having four rows disposed at 90° intervals around the circumference of the core, each row consisting of four recesses of circular cross-section. A longitudinal suction passage 16 runs along the centre line of the core 12, and the 5 base of each recess communicates with it via a respective radial passage 17. Whereas the diameter d_r of the recesses at their outer surfaces is about 4 to 6mm, the diameter of the passage is about 1mm. The reason for this difference will be apparent from the following description. A further longitudinal passage 18 runs through the core to enable it to be threaded on a guide wire. The passage 18 is defined by a conduit running coaxially within 10 the suction passage 16. At its distal end the core 12 has a tapered cone 19, to which is attached a guide member (not shown), similar or identical to the guide member 7 shown in Figure 1 and which plugs into a recess 21. At its proximal end the head 11 has a connector 20 to enable it to be connected to the wire of Bowden cable (or other control mechanism) and (if provided in addition) a suction tube.

15

The outer tube 13 is sized to be a tight but sliding fit on the main body of the core 12, and is preferably of metal, preferably of stainless steel. A plurality of openings 21 extend through the wall of the tube, and are so disposed that each can be aligned with a respective recess 15 in the core 12. As illustrated, the openings are somewhat smaller than 20 the recesses, being typically from 3 to 5mm in diameter d_o . The outer tube may be coated externally with polytetrafluoroethylene (PTFE) to ease its insertion into the oesophagus.

The assembly comprises a compression spring 30, shown in Fig. 2b. This serves to bias the core 12 in a direction away from the connector 20 and towards the cone 19, so that

the openings 21 in the outer tube 13 are aligned with the recesses 15 in the core 12. The spring 30 also keeps the Bowden cable in tension. A mechanism such as a key-way is provided (but not shown) for ensuring circumferential alignment of core 12 and tube 13. Alternatively, an eccentric bore may run longitudinally through the core, and a rod projecting 5 from the cone may then pass through the bore to provide circumferential alignment. The wire 32 of the Bowden cable is secured to the core 12 to enable control of the relative positions of the core 12 and tube 13.

In operation of the device, with the head 11, the head is introduced into the 10 oesophagus by threading a previously introduced guide wire, extending out of the patient's mouth, through the passage 18, and pushing it to the desired position using the Bowden cable 3. Accurate positioning of the device is achieved using an endoscope or x-ray imaging. In its contracted condition the oesophagus is of relatively narrow diameter, and the external diameter of the outer tube is such that it is in contact with the wall of the oesophagus over 15 most of the surface of the outer tube. Suction is then applied to the head, and this is transmitted via the longitudinal suction passage 16 and the radial passages 17 to the recesses 15 and in the core 12 and the openings 21 in the outer tube 13. At this stage the recesses 15 and openings 21 are aligned with one another. The suction draws into each recess a piece of the tissue nearest the surface of the oesophagus, namely the mucosa and submucosa. The 20 recesses are made sufficiently shallow that deep muscle tissue is not drawn in. The handle is then used to operate the Bowden cable, causing the core 12 to move longitudinally relative to the outer tube 13 towards the connector 20. This takes the openings 21 out of alignment with the recesses 15, and the resulting shearing action severs the drawn-in tissue portions from the remainder of the oesophagus, so giving one biopsy in each recess. The core 12 is

then kept in this new position, so that the biopsies remain securely in the recesses. The head is then withdrawn from the patient's body.

Once the cutting head is withdrawn from the body, the outer tube is moved back to 5 its original position and the biopsies are then transferred from the cutting head for examination. This transfer should be effected in such a way as to retain the information which their position in particular recesses provides, as to whereabouts in the oesophagus each came from. This can be achieved, or assisted, in various ways. Thus, the split sleeve 40 shown in Figs. 2e and 2f can be slid over the outer tube before the removal procedure starts, 10 to cover up three of the four rows of recesses. Each row of biopsies can then be removed, and appropriately labelled, separately. Another possibility is to wrap around the outer tube a piece of absorbent paper or similar material, for example cellulose acetate, hold it in place, for example, using a clam-shell design of clamp, and then apply a blowing action, in place of suction, in the longitudinal passage 16 to transfer the biopsies to the paper. As an 15 alternative to blowing, a device may be provided for insertion inside the cutting head to push the biopsies out. The paper can be pre-marked with indicia so that each biopsy is located next to a respective indicium.

In Figures 3a and 3b, the head 11 is shown in greater detail in cross section. The 20 same reference numerals are used as in Fig. 2. As shown, the wire 32 of the Bowden cable is connected to core 12 and the sheath 34 is connected via the connector 20 to the outer tube 13. Suction is provided to the suction passage 16 by a suction tube 40.

A conduit 36 running within the suction passage 16 provides the passage 18 through 25 which a guide wire can be threaded. The conduit 36 comprises part of the cone 19 and is

a tight fit in the hole in the connector 20, and grease may be added to further ensure that suction is not lost past the outside of the conduit. When the cutting head is operated via the Bowden cable the spring 30 is compressed, and the head assumes the configuration shown in Figure 3b.

5

As described above, the force required to move the core 12 relative to the outer tube 13 is provided by the Bowden cable. However, it could alternatively be provided by other means, such as a pre-loaded spring or an hydraulic piston.

10

Figure 4 shows an alternative arrangement for the head 11 in which the outer tube 13 is slidably received over the core 12, so that the core 12 remains stationary with respect to the connector 20 and the cone 19. Furthermore, the force for movement of the outer tube 13 is provided by a pre-compressed spring 30a, shown as a spring washer in Figure 4. A detent pin 31 is released to enable the stored energy in the spring 30a to provide movement of the outer tube 13 into a new position (not shown) in which the openings 21 are out of alignment with the recesses 15. The detent pin 31 may be released using the Bowden cable, or another arrangement which may enable the Bowden cable to be omitted.

15

A further alternative form of cutting head is shown in Figure 5. In most respects it is the same as that of Figure 2, and so will not be described here in detail. Integers in Figure 5 corresponding to integers of Fig. 2 are again denoted by the same reference numerals, but with the addition of 100. The difference is that rather than relying on a shearing action to sever the biopsies, the core is provided with blades 50 each held in a respective groove 51. The cross-section of Fig. 5c shows a blade 50 in one of the grooves 51. In practice, there would, of course, be blades in all of them. As a consequence of the

positioning of the blades, the device of Figure 5 achieves its cutting action by having the core 112 and tube 113 rotate with respect to one another rather than move longitudinally. For this purpose, these two components are rotationally biassed with respect to one another by a torsion spring and relative movement occurs in response to operation of a trigger.

5

The cutting head used in the present invention may be made sterilisable for reuse, though preferably it is disposable, since sterilising such cables may be difficult.

An important feature of the present invention is the ability to take a number of 10 biopsies simultaneously whose position relative to one another in the oesophagus is known. In order also to be able to take the biopsies from given locations in the oesophagus, it is important to be able to orientate the cutting head to a desired position in the oesophagus. For this purpose, it is desirable for the outer sheath of the Bowden cable to be relatively stiff as regards torque transmission, whilst remaining flexible in terms of its ability to bend. 15 Techniques for achieving this are known in the field of endoscopes, involving winding two helical coils, of opposite hand, around the endoscope, and these techniques can be employed here. Orientation can be assisted by inserting a mouth guard between the patient's teeth, the guard having a mark on it for alignment with a line extending along the length of the Bowden cable parallel to its longitudinal axis. Alternatively, or additionally, the cutting head 20 can be provided with a marker, for example, a coloured arrow, which can be oriented to line up with the arrow normally provided in the viewing window of an endoscope.

The device is described above on the basis that it would be used in front of a conventional endoscope. However, an alternative possibility would be for the cutting head 25 and Bowden cable to be small enough to pass through a large channel endoscope. Another

possibility would be to make the device annular so that it could fit over an endoscope.

For ease of manufacturing of the cutting head, one possibility is to assemble it from a plurality of sections connected end to end. One such section is shown in Figure 6, but 5 which relies upon a longitudinal cutting action rather than the rotational cutting action described with reference to Figure 5. Therefore, control of the head using sections as shown in Figure 6 may be achieved in the manner described with reference to Figures 2 to 4. When the cutting action is provided by blades, each section can be made entirely of plastic, except for the blades. In Figure 6 each section comprises an annular blade 60 held in a 10 mounting 61. Openings 62 are defined in the mounting which form the recesses into which the samples are drawn. The sections are bonded together to form the core. Each opening 62 has a wide part 62a corresponding to the recesses 15 in the embodiments described with reference to Figures 2 to 4, and a narrow part 62b corresponding to the passage 17. The narrow part 62b allows suction of tissue.

15

It is also possible that a plurality of cutting heads could be connected to each other in articulated fashion, to improve ease of insertion into the patient, with each section being shorter than would otherwise be the case.

20

Finally, mention should be made of the fact that instead of taking biopsies, the device of the invention could be used for other purposes, for example, shaving off the mucosa from a section of the oesophagus.

CLAIMS

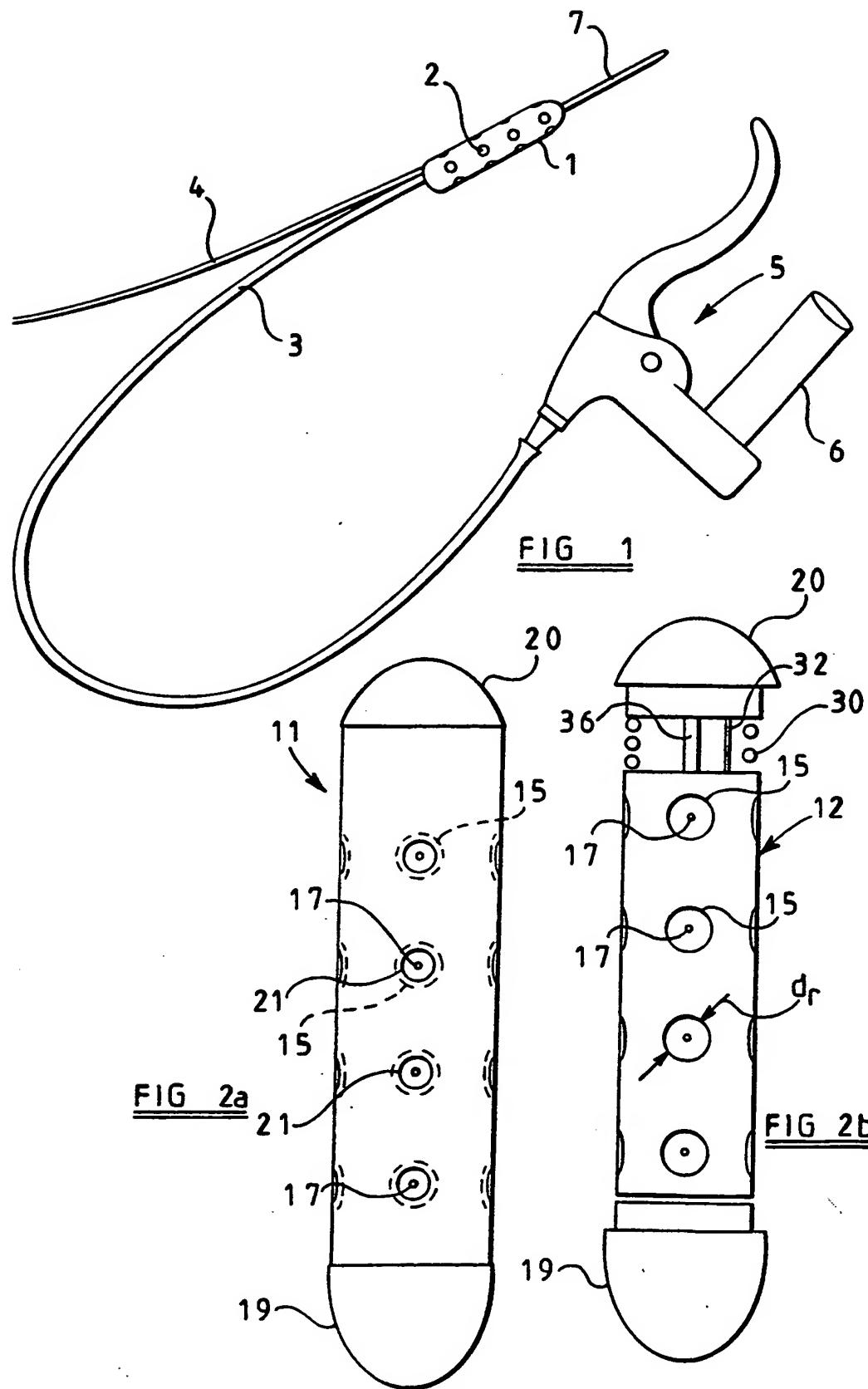
1. A device for taking biopsies, which comprises a cutting head having a surface in which are defined a plurality of recesses, means for communicating suction to the recesses to draw tissue therein, and means for severing the drawn in tissue to form biopsies each of which is held in a respective recess.
5
2. A device as claimed in claim 1, wherein the recesses are arranged in rows with the recesses in each row being aligned axially with the corresponding recesses in the other rows.
10
3. A device as claimed in claim 1 or 2, wherein the cutting head comprises a core which includes the recesses for holding the biopsies and an outer sheath which includes a plurality of openings for cooperation with the recesses, the core and the sheath being axially slidably with respect to each other to perform the severing operation.
15
4. A device as claimed in claim 3, wherein one end of the cutting head is attached to the distal end of a cable which controls the severing operation.
20
5. A device as claimed in claim 4, wherein the proximal end of the cable is connected to a handle which is operable to perform the severing operation.
25
6. A device as claimed in claim 4 or 5, wherein the proximal end of the cutting head is connected to a tube for carrying suction to the head.
7. A device as claimed in any one of claims 3 to 6, wherein the recesses in the core

comprise a first radially outer portion of a first diameter, and a second radially inner portion of a second, smaller diameter, the radially inner portions communicating with a central passageway within the core to which suction is provided.

5 8. A device as claimed in any one of claims 3 to 7, wherein the openings in the sheath have a smaller diameter than the maximum diameter of the recesses.

9. A device as claimed in any one of claims 3 to 8, wherein the sheath is biased with respect to the core into a position in which the openings 21 in the sheath are aligned with the 10 recesses in the core.

1 / 3



2 / 3

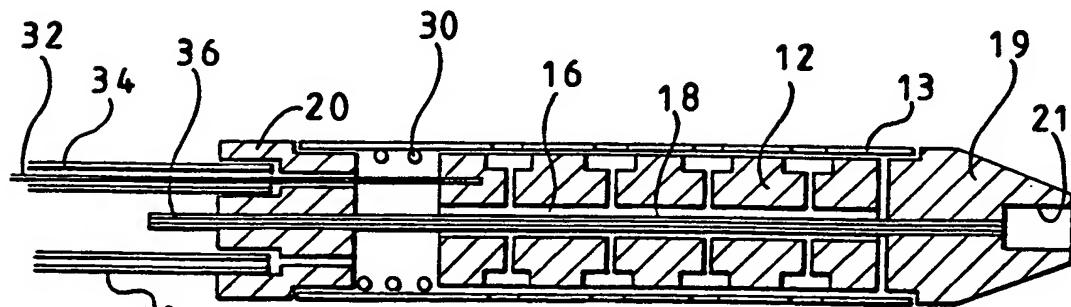
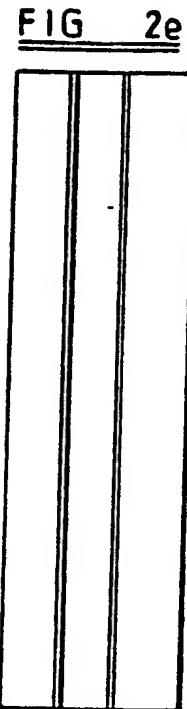
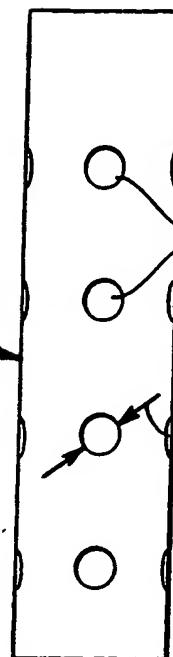
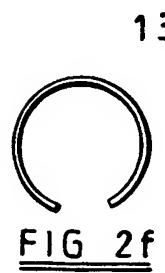
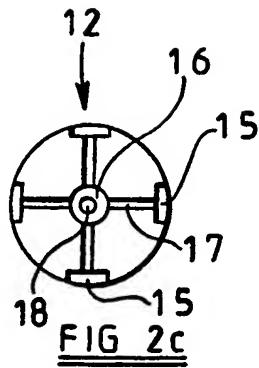


FIG 3a

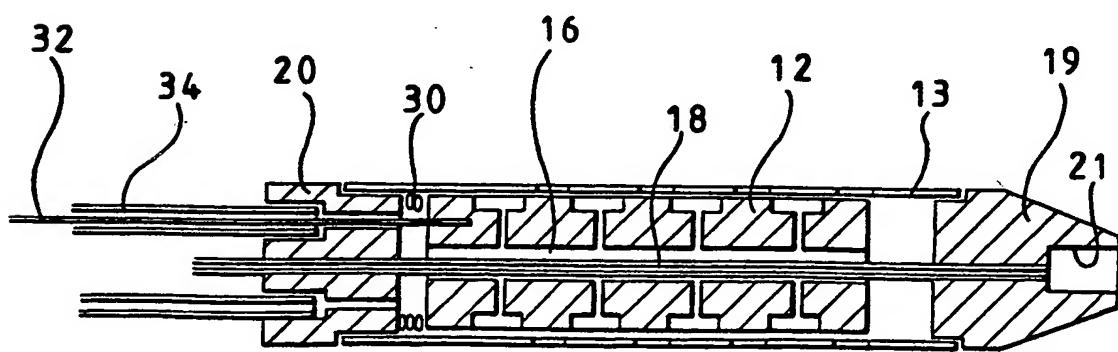
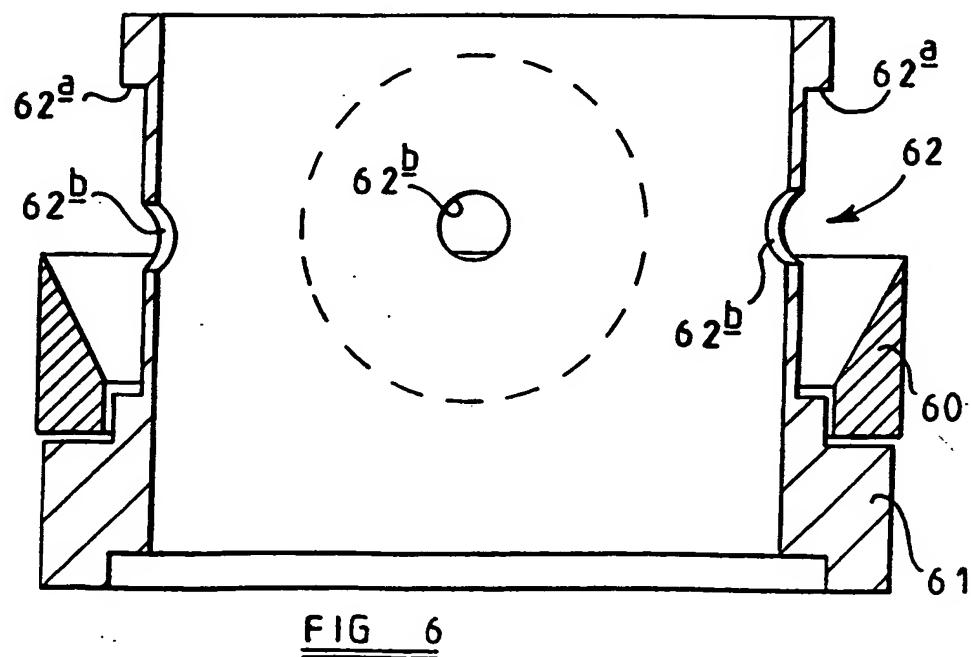
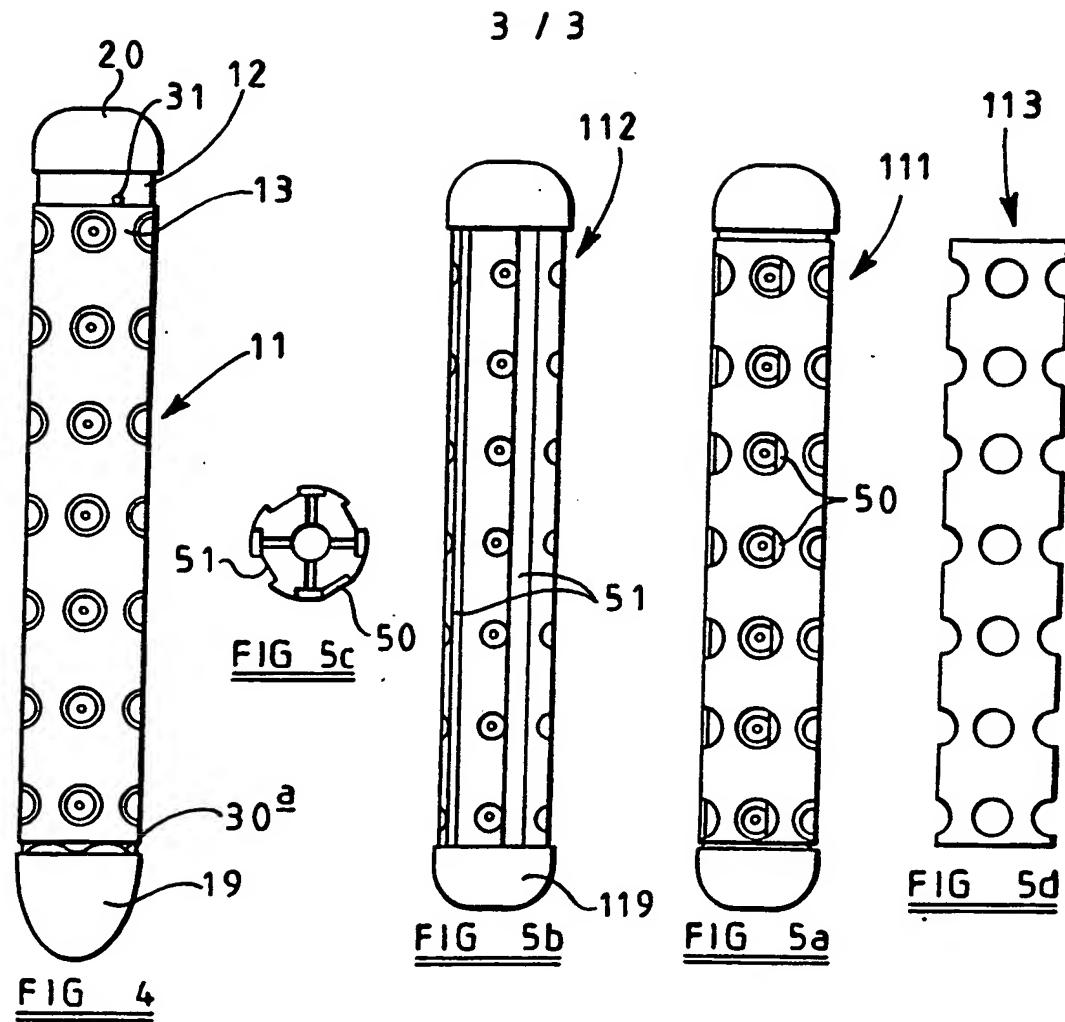


FIG 3b



INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B10/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 458 112 A (WEAVER GEORGE W) 17 October 1995 (1995-10-17) column 6, line 25 - line 35; figures 6,7	1-6
A	US 5 106 364 A (HAYAFUJI MINEKI ET AL) 21 April 1992 (1992-04-21) column 7, line 29 - line 37; figures 5,14	7-9
X	US 5 409 012 A (SAHATJIAN RONALD A) 25 April 1995 (1995-04-25) column 3, line 60 - line 64; figure 3	1,2
A	WO 96 24289 A (BIOPSYS MEDICAL INC) 15 August 1996 (1996-08-15) page 20, line 1 - line 11; figure 6	1,6
A	US 5 409 012 A (SAHATJIAN RONALD A) 25 April 1995 (1995-04-25) column 3, line 60 - line 64; figure 3	1
		-/-

Further documents are listed in the continuation of box C.

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INTERNATIONAL SEARCH REPORT

Int. national Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 454 887 A (KRUEGER CHRISTIAN) 19 June 1984 (1984-06-19) column 3, line 13 – line 24; figures 3,4	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00177

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 5458112	A	17-10-1995	NONE		
US 5106364	A	21-04-1992	JP	3039155 A	20-02-1991
			JP	3039157 A	20-02-1991
WO 9624289	A	15-08-1996	US	5649547 A	22-07-1997
			CA	2211422 A	15-08-1996
			EP	0808129 A	26-11-1997
			JP	10513384 T	22-12-1998
US 5409012	A	25-04-1995	CA	2179898 A	06-07-1995
			CA	2180138 A	06-07-1995
			EP	0746226 A	11-12-1996
			EP	0746227 A	11-12-1996
			JP	9509588 T	30-09-1997
			JP	9507142 T	22-07-1997
			WO	9517847 A	06-07-1995
			WO	9517849 A	06-07-1995
			US	5533516 A	09-07-1996
US 4454887	A	19-06-1984	DE	3115192 A	04-11-1982
			AR	228898 A	29-04-1983
			AT	129782 A	15-06-1991
			AU	8265782 A	21-10-1982
			BE	892831 A	02-08-1982
			BR	8202191 A	29-03-1983
			CH	658587 A	28-11-1986
			DD	202244 A	07-09-1983
			DK	169182 A	16-10-1982
			FI	821254 A	16-10-1982
			FR	2504012 A	22-10-1982
			GB	2096467 A, B	20-10-1982
			IL	65495 A	30-04-1985
			IT	1218319 B	12-04-1990
			JP	57177771 A	01-11-1982
			NL	8201545 A	01-11-1982
			NO	821215 A	18-10-1982
			PT	74738 A, B	01-05-1982
			SE	456481 B	10-10-1988
			SE	8202173 A	16-10-1982
			ZA	8202508 A	30-03-1983

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